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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,441	SZYMCZAK ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-28* is/are pending in the application.

4a) Of the above claim(s) *6,18,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-14, 16-17, 19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In view of the Appeal Brief filed on December 22, 2003, PROSECUTION IS HEREBY REOPENED. New grounds of rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-2, 4-8 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising compressible admixture of simethicone and silicified microcrystalline cellulose and magnesium aluminometasilicate, does not reasonably provide enablement for a composition comprising "admixture of simethicone and an adsorbent". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention relates to a composition comprising admixture of simethicone and an absorbent and optionally active ingredients (e.g., bisacodyl, famotidine, prucalopride, diphenoxylate, etc...), wherein the weight ratio of simethicone to adsorbent is at least about 1:2.22.

(2) The state of the prior art

The art recognizes difficulties in preparing solid simethicone dosage forms, particularly for direct compression tableting, so that the tablet will withstand the rigors of further processing and compaction. To achieve sufficient flowability for processing and sufficient cohesion for compaction, various excipient materials alone or in mixtures (e.g., magnesium aluminate metasilicate, aluminum silicate, magenisum silicate, calcium silicate, carboxymethylcellulose, hydroxypropyl methylcellulose, maltodextrin, dextrin, anhydrous tribasic calcium phosphate, dibasic calcium, microcrystalline cellulose and

colloidal silicon dioxide, etc...) have been incorporated to simethicone (See, page 1, para. 5 thru page 3, para. 9 of the instant specification).

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high.

(5) The breadth of the claims

The instant specification defines that the instant adsorbent refers to "a solid material or combination of solid materials that is capable of adsorbing and carrying an oily or fluid material". The claims are very broad due to the vast number of possible compounds of that are described as being an adsorbent. The scope of instant claims encompasses colloidal silicon dioxide, silicas, activated alumina, cellulosic materials, calcium oxide, calcium sulfate, clay materials, cyclodextrin, calcium phosphate, keratin solid fiber, activated charcoal and etc... (See US 4711774; US 4855268; JP 0288425; WO 9965822; US 20030054037; US 5449521; US 4772627; US 5475150; Remington's Pharmaceutical Sciences, A. R. Gennaro (ed.), Mack Publishing Company, pp. 774-778 (1990); US 4716033; US 4727824; US 4083965; US 6270793).

(6) The amount of direction or guidance presented & (7) The presence or absence of working examples

The specification discloses that using silicified microcrystalline cellulose and magnesium aluminometasilicate as substrates onto which simethicone and/or liquid active is adsorbed provides a free-flowing composition containing simethicone for forming a solid dosage form that contains either larger weight percentages of simethicone

while maintaining substantially the same size than previously possible or the same weight percentage of simethicone in a smaller size (page 3, para. 11). It appears in view of the instant specification that the instant invention is entirely based on applicant's alleged discovery of using silicified microcrystalline cellulose and magenisum aluminometasilicate as suitable adsorbent in the specific weight ratio of simethicone to adsorbent, "at least about 1:2.22", in improving tablet workability.

As discussed above, the specification provides only example of using silicified microcrystalline cellulose and magnesium aluminometasilicate as a suitable adsorbent for improving tablet workability of simethicone. Numerous possible "adsorbents" that are potentially suitable for the instant invention are not necessarily structurally related to each other, and the skill artisan would have not known that which "adsorbents" would behave similarly to silicified microcrystalline cellulose and magnesium aluminometasilicate mixture and are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation. As stated above, the instantly claimed "adsorbent" read on all or any compounds that are capable of "adsorbing and carrying an oily or fluid material", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the

direction in which the experimentation should proceed." In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of "adsorbent" that would be enabled in this specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites that the weight ratio of simethicone to adsorbent is "at least about 1:2.00". The scope of the instant claim 2 encompasses "1:1.95, 1:1.96, 1:9.7, 1:9.8, 1:9.9, 1:2.00, 1:2.01, 1:2.02, 1:2.02, 1:2.03, 1:2.04, 1:2.05...1:2.20, 1:2.21...". The scope of the claim 2, for example "1:1.95, 1:1.96, 1:9.7, 1:9.8, 1:9.9, 1:2.00, 1:2.01, 1:2.02, 1:2.03, 1:2.04, 1:2.05", is broader than the scope of the claim 1, "at least about 1:2.22", for example "1:2.20, 1:2.21, 1:2.22, 1:2.23, 1:2.24, 1:2:25, 1:2:26, 1:2.27, 1:2.28, 1:2.29, 1:2.30...". As discussed above, claim 2 fails to further limit the subject matter of the claim 1. This inconsistency leads to lack of clarity of the claims as a whole.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens et al. (US 5679376 A).

With respective to claims 1-2,

Stevens teaches a solid oral dosage form comprising loperamide, simethicone, microcrystalline cellulose, colloidal silicon dioxide and dibasic calcium phosphate, wherein a ratio of simethicone and microcrystalline cellulose is about 1:2.12 (125mg:265.5mg); a ratio of simethicone and a combination of colloidal silicon dioxide and microcrystalline cellulose is about 1:2.37 (125mg:297mg); and a ratio of simethicone and a combination of colloidal silicon dioxide, microcrystalline cellulose and dibasic calcium phosphate is about 1:5.34 (125mg:667mg). See table in column 9, page 65 thru column 10, page 10.

Although the reference is silent about the use of microcrystalline cellulose or colloidal silicon dioxide or dibasic calcium phosphate as an adsorbent, the use of microcrystalline cellulose as a diluent, adsorbent, lubricant or disintegrant or the use of colloidal silicon dioxide or dibasic calcium phosphate as an adsorbent, glidant or disintegrant is notoriously known for the skilled artisan. In other words, such adsorbent characteristic or property must be an inherent function of microcrystalline cellulose or colloidal silicon dioxide or dibasic calcium phosphate. Since the instantly claimed "adsorbant" or "adsorbent" (see the definition of term "adsorbant" in page 10, lines 1-5

of the specification) refers to either single "solid material" or combination of "solid materials", the referenced composition anticipates the claimed invention.

Since the referenced ratios of 1:2.12 (simethicone to microcrystalline cellulose) or 1:2.37 (simethicone to the combination of microcrystalline cellulose and colloidal silicon dioxide) or 1:5.34 (simethicone to the combination of microcrystalline cellulose, colloidal silicon dioxide and dibasic calcium phosphate combination) "metes and bounds" the claimed "at least about 1:2.22", Stevens anticipates the claimed invention.

With respective to claims 4-5,

Stevens expressly teaches that active ingredients for said solid oral dosage form are selected from the group consisting of cimetidine, ranitidine, famotidine, diphenoxylate, loperamide and loperamide-N-oxide (abstracts and claims).

Although famotidine and diphenoxylate are not specifically named in Examples, one of ordinary skill in the art must be able to be "at once envisaged" from the small number of disclosed species. Therefore, the reference clearly anticipates the claimed invention.

5. Claims 1-2, 4-5, 7-8 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Luber et al. (US 6103260 A).

With respect to claims 1-2,

Luber teaches an antifoam oral solid dosage form preparations formed from a free glowing granular composition comprising an admixture of simethicone and and either one or both of granular anhydrous tribasic calcium phosphate or dibasic calcium

phosphate, wherein the simethicone is adsorbed by the granular anhydrous tribasic or dibasic calcium phosphate or mixture thereof; and wherein ratios of simethicone to granular tricalcium phosphate are 1:3.5 in Examples 1-2 and 1:4 in Example 6.

Although Luber is silent about the use of granular anhydrous tribasic calcium phosphate or dibasic calcium dibasic calcium phosphate as an adsorbent, such characteristic or property must be inherently presented in said composition (claims 1 and 7). The instant specification defines that adsorbent means a solid material or combination of solid materials that is capable of adsorbing and carrying an oily or fluid material, such as simethicone, while retaining sufficient flowability to assure content uniformity and sufficient compactability to be processed into tablets using direct compression methods (page 10, lines 1-5). Since the claims do not recite any specific adsorbent(s) in a composition, the referenced granular anhydrous tribasic or dibasic calcium phosphate or mixture falls within the broadly defined "adsorbent". Thus, the reference clearly anticipates the claimed invention.

Regarding the claimed weight ratio of simethicone to "adsorbant" such as "at least about 1:2.22" or "at least about 1:2.00", the referenced examples (1:3.5 in Examples 1-2 and 1:4 in Example 6) clearly falls within the claimed ratio. Therefore, the reference clearly anticipates the claimed invention.

With respect to claims 4-5,

Luber also teaches that said oral solid dosage form further comprises additional active ingredients selected from H2 receptor antagonists (i.e., famotidine) and antidiarrehal agents (i.e., loperamide and diphenoxylate). See claims 7-8 and column 5,

lines 18-21. One of ordinary skill in the art must be able to be "at once envisaged" from the small number of disclosed species. Therefore, the reference clearly anticipates the claimed invention.

With respect to claims 7-8,

Luber also teaches that the amount of simethicone in the final composition is 10% to 70%, typically 10% to 50% (column 3, lines 39-40 and column 4, lines 45-50). Since the referenced simethicone concentration falls within the claimed "at least 30% wt simethicone" in claim 7 or "from about 31 wt% to about 35 wt% simethicone" in claim 8, the reference clearly anticipates the claimed invention.

With respect to claims 11-12,

Luber also teaches various ranges of "Hardness" (i.e., 8-10 kp in Example 3; 11-12 kp in Example 4; 8-9 kp in Example 5; 6-14kp in Example 6). Since the referenced "Hardness" value falls within the claimed "a hardness value of at least 2 kp/cm2" and "a harness value of from about 5 to about 10 kp/cm2", the reference clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 3, 9-10, 13-14, 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitsusho Yakuhin Kogyo KK (JP 398241) in view of Tobyn et al. (International Journal of Pharmaceutics 169 (1998) 183-194).

The claims read on a composition comprising an admixture of simethicone, silicified microcrystalline cellulose, and magnesium aluminometasilicates. Further limitations include a) the specific weight ratio of simethicone to a combination of silicified microcrystalline cellulose and magnesium aluminometasilicates; b) the specific concentration of simethicone; c) the specific dosage concentrations of silicified

microcrystalline cellulose and magnesium aluminometasilicates; and d) a hardness value of a tablet.

Kitsusho Yakuhin Kogyo KK teaches a method for preparing simethicone tablets by mixing and granulating simethicone with magnesium aluminum metasilicate. In particular, the formulation disclosed by the above Japanese patent requires at most 25% simethicone and 75% or greater silicate, binder (i.e., starch and lactose) and dispersing agents (i.e., carboxymethylcellulose). Further, the reference teaches that when the amount of simethicone exceeds 25%, there is tendency that a portion of the simethicone can be carried away, therefore the tablet workability is not desirable.

Tobyn discloses the advantage of using silicified microcrystalline cellulose in improving tablet workability such as "powder flow", "tablet strength", "lubricant sensitivity" and "wet granulation" (page 184, column 2, lines 4-9; page 193, column 2, lines 43-48).

The teaching of Kitsusho Yakuhin Kogyo KK differs from the claimed invention in i) the incorporation of silicified microcrystalline cellulose in said composition; ii) "at least 30 wt% simethicone" in said composition; iii) the specific amounts of silicified microcrystalline cellulose and magnesium aluminometasilicates in said composition; and iv) the specific harness value of the tablet. To incorporate such teaching into the teaching of Kitsusho Yakuhin Kogyo KK, would have been obvious in view of Tobyn who teaches the advantage of using silicified microcrystalline cellulose as a pharmaceutical excipients to improve powder flow characteristic, lubricant sensitivity, tablet strength and better bulk physical properties.

One having ordinary skill in the art would have been motivated, with a reasonable expectation of success, to incorporate silicified microcrystalline cellulose having good free-flowing and disintegrating properties (which is relatively new pharmaceutical excipients in the art) such that the tablet workability would be significantly improved. Furthermore, one having ordinary skill in the art would have been motivated to increase the amount of simethicone above 25% in the solid final blend for tabletting by incorporating silicified microcrystalline cellulose in said composition.

Although the prior art references are silent about the specific dosage amounts of active ingredients and the hardness value of tablet, the optimization of amounts of kwon active and inactive ingredients in a composition or the determination of optimum hardness value of the tablet is well considered within the skill of the artisan, absent evidence to the contrary.

7. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitsusho Yakuhin Kogyo KK (JP 398241) in view of Tobyn et al. (International Journal of Pharmaceuitcs 169 (1998) 183-194) and Stevens et al. (US 5679376).

The modified teaching of Kitsusho Yakuhin Kogyo KK includes all that is recited in claims 16 and 17 except for the incorporation of active pharmaceutical ingredients such as famotidine. Stevens teaches or suggests the use of simethicone and other pharmaceutical excipients in preparing oral solid dosage form containing H2 blockers (e.g,, famotidine). One having ordinary skill in the art would have known that simethicone is routinely combined with H2 blockers such as famotidine in solid oral dosage formulation art, and would have been motivated to further modify the teaching of

Kitsusho Yakuhin Kogyo KK such that the better solid oral dosage form containing famotidine would be formulated. One having ordinary skill in the art would have been motivated to do this so that the tablet workability would be significantly improved.

Conclusion

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614